1. Immunity
    a. Ability to resist damage from foreign substances (microorganisms, harmful chemicals).
    b. Categorized as being innate or adaptive.
2. Innate immune system
    a. Provides the basic means for the destruction of foreign organisms.
    b. Recognizes and destroys certain foreign substances, but the response to them is the same during each encounter.
    c. Consists of mechanical barriers as well as certain cells and chemical mediators.
    d. Main barriers are skin and mucosae.
    e. Cells and chemicals include granulocytes, monocytes, macrophages, antimicrobial proteins, etc.
    f. A characteristic response of the innate system is inflammation.
3. Adaptive immune system
    a. Consists of cells that attack particular antigens in a particular way.
    b. Improves and enhances the efficiency of the innate mechanisms and remembers the infection the next time it is encountered.
    c. Specificity (the ability to distinguish pathogens) and memory (the ability to respond more rapidly to a previously encountered pathogen) are characteristics of adaptive immunity.
4. Skin
    a. Repels pathogens in many ways.
    b. Highly keratinized, which provides a physical barrier to pathogens.
    c. Acidity of sweat can kill some pathogens.
    d. Sebum is bactericidal.
5. Mucous membranes
    a. Line the digestive, respiratory, urinary, and reproductive tracts - all of which are potential entrance points for pathogens.
    b. Often covered in sticky, pathogen-trapping mucus.
    c. Respiratory mucosa is also ciliated. Cilia sweep bacteria-laden mucus upward to the pharynx where it can be swallowed. Coughing and sneezing also assist in expulsion.
6. Body fluids also provide innate defense
    a. Tears, saliva, and urine wash away microorganisms.
    b. Saliva, intestinal fluid, and tears contain lysozyme, an enzyme that destroys bacteria.
    c. Acidity of certain mucosal secretions (gastric and vaginal) can impair pathogens.
7. Bacterial competition
    a. Growth of disease-causing organisms is inhibited by the growth of non-pathogenic bacteria in the gastrointestinal and urogenital tracts. These bacteria successfully compete w/ the pathogenic ones for nutrients and resources.
8. WBCs and derivatives
    a. The most important cellular component of the innate immune system.
    b. Can exit blood vessels (diapedesis), converge upon areas of infection/damage (positive chemotaxis) and move over, btwn, and through other cells.
9. Neutrophils
    a. Small phagocytic cells that are the first to enter infected tissues and function primarily as bacteria killers.
10. Macrophages
    a. Large phagocytic cells derived from monocytes.
    b. Free (able to move thru tissue spaces) such as the alveolar macrophages in the lungs or fixed (permanent residents of a particular organ) such as the microglia of the CNS.
    c. Perform phagocytosis whereby they ingest something (a bacterium, particulate matter, etc.) and enclose it within a membrane-bound vesicle.
        i. Begins with the adherence of a microbe to the phagocyte. The probability of this occurring is increased when antibodies or complement proteins have already bound to the microbe (a process called opsonization).
        ii. Phagocyte then extends membrane "arms" that wrap the microbe and engulf it, forming a membrane-bound vesicle containing the pathogen. This vesicle is known as a phagosome.

iii. The phagosome then will fuse with a lysosome, an organelle that contains digestive enzymes.
iv. The enzymes will then destroy the engulfed material.
v. Whatever indigestible material remains is then exocytosed.

11. Natural killer cells
    a. Specialized type of lymphocyte that attacks and destroys virus-infected cells and cancer cells.
12. Antimicrobial proteins
    a. Interferons.
        i. Proteins produced by cells that have been infected with a virus.
        ii. Diffuse to nearby cells and stimulate them to synthesize a protein that prevents viral replication. This prevents copies of the original virus from taking over neighboring cells.
        iii. Do not save the infected cell but prevent nearby cells from being infected.
        iv. The same interferons can act against many different types of viruses.
    b. Complement system
        i. Refers to a group of about 20 plasma proteins synthesized by the liver.
        ii. Normally found in the blood in an inactive state.
        iii. May be activated by interacting directly with a pathogen or by members of the adaptive immune system. Activation of complement results in 4 things:
            1. Chemotaxis – activated complement proteins attract WBCs.
            2. Opsonization → binding of activated complement proteins to bacteria increases the likelihood of their phagocytosis.
            3. Inflammation → activated complement proteins bind to basophils and mast cells and stimulate histamine release. This results in vasodilation and increased capillary permeability and inflammation.
            4. Lysis → activated complement proteins can form a "membrane attack complex," which is a tube that pierces the bacterial cell membrane. This allows salt and water to flow in and results in cell lysis.
13. Inflammatory response
    a. Occurs whenever tissues are damaged.
    b. Helps to prevent pathogen spread, disposes of pathogens/debris, and allows for repair.
    c. Signs include *heat, redness, swelling, pain, and loss of function*.
    d. Begins when damaged tissues release inflammatory chemicals (histamine, prostaglandins, leukotrienes, kinins, etc.).
        i. These act to: increase WBC count, increase local capillary permeability, cause local vasodilation, attract WBCs to the injury site, and stimulate pain-sensitive neurons.
        ii. Increase in vasodilation and capillary permeability yields an increase in blood flow and capillary fluid loss. This results in swelling, heat, redness, and increased access to the injury site by WBCs, complement proteins, antibodies, and clotting proteins.
14. Fever
    a. Systemic response to infection associated with an abnormally high body temperature.
    b. Many WBCs and macrophages release chemicals called pyrogens in response to pathogen exposure.
    c. Pyrogens act on the body's hypothalamic thermostat to raise body temperature.
    d. Mild increase in temperature can accelerate WBC function; impair bacterial metabolism; and cause the liver and spleen to sequester zinc and iron, 2 minerals necessary for bacterial survival.
    e. Major increase in body temperature can result in severe protein denaturation and possible loss of life.
15. Adaptive immune system
    a. Responds in strong ways tailored to particular antigens.
    b. Differs from the innate system in that it's specific, systemic, and improves its efficiency each time it encounters the same pathogen.

16. Antigens
    a. Substances that can provoke the adaptive immune system and cause a response.
    b. Large, complex molecules not normally found in the body. (Non-self/foreign antigens.)
    c. Haptens are small, foreign molecules that do not generate an immune response unless they are attached to a normal body protein.
    d. Self-antigens are molecules produced by the body that stimulate the adaptive immune system. They can result in autoimmune disease.
17. Lymphocytes
    a. Principal cells of adaptive immunity are the lymphocytes.
    b. 2 main types: B lymphocytes and T lymphocytes.
    c. Both are formed initially in the red bone marrow.
    d. B lymphocytes gain immunocompetence (i.e., mature) in the bone marrow.
    e. T lymphocytes gain immunocompetence in the thymus.
    f. Immunocompetent B and T cells are composed of small groups of identical lymphocytes called clones.
    g. Each clone has many copies (10^4-10^6) of a receptor on its cell surface. The presence of one specific type of receptor allows each clone to bind/recognize and interact with 1 specific type of antigen.
    h. There are more than a million different varieties of clones, giving the lymphocytes a large variety of antigens to which they can respond.
    i. Once a B or T cell has become immunocompetent, the naïve cells will travel to the lymph nodes, spleen, or other lymphoid organs to await antigens.
18. Antigen-presenting cells
    a. Dendritic cells in connective tissue, and the macrophages.
    b. Function by engulfing antigens and then presenting antigen fragments on their surface as a signal to Helper T cells (a type of T lymphocyte).
    c. Identifying the invading antigens and then displaying it to the specific appropriate lymphocyte and saying – "*Hey these invaded us. Find them, build an army, & kill 'em!*"
19. Components of the adaptive response
    a. Antibody-mediated immunity and cell-mediated immunity.
    b. Antibody-mediated response (a.k.a. the humoral response) is the body's response to extracellular antigens, i.e., those antigens found within plasma, ISF, or lymph.
    c. Cell-mediated immunity refers to how the body deals with microorganisms that have invaded cells (e.g., viruses, certain bacteria and fungi).
    d. 2 branches will overlap and work together.
20. Adaptive immune scenario (Antibody-mediated response)
    a. Suppose a pathogen has invaded the body and is somewhere in the extracellular space (i.e., plasma, lymph, tissue fluid, etc).
    b. 1st step in the response is for an APC (i.e., a macrophage or dendritic cell) to engulf it.
    c. Once engulfed, the pathogen will be destroyed. Then resulting pieces (antigens) will be displayed on the surface of the APC by a molecule known as a class II MHC protein.
    d. Antigen will be recognized by and stimulate a Helper T cell that contains the specific receptor matching the particular antigen.
    e. Helper T cell also receives a confirmation signal from the APC before it proceeds. This confirmation signal is called costimulation.
    f. Helper T cell now proliferates to form many more Helper T cells, which also respond to the same original antigen. These Helper T cells can release cytokines (which are chemicals that will stimulate the body's innate defenses). The Helper T cells will also help activate B cells and/or Killer T cells.
    g. Now suppose that the same pathogen runs into a B cell that carries the specific receptor.
    h. The B cell will engulf it, kill it, and display antigens on its own MHC II proteins.
    i. Once the antigen has been displayed to the previously mentioned Helper T cells, those Helper T cells will stimulate the B cell to begin dividing.
    j. Most of the resulting cells will be plasma cells.
    k. Plasma cells secrete up to 2000 antibodies per second.
    l. Each antibody will specifically bind to the original antigen and mark it for destruction.

m. A small percentage of the clones will be memory cells.
n. These memory cells have the ability to mount an almost immediate response if the same antigen appears again in the future.
o. NB: this entire process is referred to as clonal selection.

21. Antibodies
    a. Also called immunoglobulins, gamma globulins, or Ig's.
    b. Each consists of 4 polypeptide chains that combine to form a Y-shaped structure known as an antibody monomer.
    c. Each antibody monomer has 2 variable regions (the ends of the 2 arms of the Y) and a constant region (the stem of the Y).
    d. Variable regions contain the antigen-binding sites. All antibodies released from the same plasma cell will have the same antigen-binding sites. Thus they will all be specific for the same antigen.
    e. Constant region binds to other immune chemicals or cells and *determines the mechanism by which the bound antigen will be destroyed*. The constant regions also determine the antibody class. There are 5 antibody classes: IgM, IgA, IgD, IgG, and IgE. Antibodies of each class have different constant regions and different roles and locations in the body.
    f. Antibodies have 4 main mechanisms of action: precipitation, lysis, agglutination, and neutralization.
    g. Precipitation
        i. Occurs when antibodies bind soluble antigens into clumps. This increases the likelihood of phagocytosis.
    h. Lysis
        i. Occurs when antibodies activate complement. This results in the formation of a membrane attack complex, and bursting of the bacterial cell.
    i. Agglutination
        i. Occurs when antibodies bind cell-bound antigens into clumps. This increases the likelihood of phagocytosis.
    j. Neutralization
        i. Occurs when antibodies bind to and mask the dangerous portions of antigens, toxins, and viruses.
22. Adaptive immune scenario (Cell-mediated response)
    a. Now suppose that the original pathogen has begun invading the body cells.
    b. Antibodies are only effective against extracellular antigens. They're useless against pathogens that have slipped inside body cells.
    c. Fragments of intracellular proteins are displayed on the surface of every nucleated body cell by molecules known as class I MHC proteins.
        i. This gives a "window" into a cell, that T lymphocytes can "look in" to see if everything is ok.
    d. The combination of our original antigen and the MHC I protein displaying it will bind to and stimulate a Killer T cell that contains the specific receptor matching the original antigen.
    e. With a little stimulation from our aforementioned Helper T cells, the activated Killer T cell will begin to divide. This results in both mature killer T cells and memory killer T cells.
        i. Memory killer T cells will persist in case of a subsequent infection by the same pathogen.
        ii. Mature killer T cells will set about to kill those body cells displaying the same specific antigen as the original one that began the activation process, e.g., cells infected by the same type of virus. Killer T cells release lethal chemicals that are capable of causing cell death.
23. Primary vs. Secondary immunes responses
    a. The initial encounter with a particular antigen is termed the primary immune response.
    b. It typically has a lag period of 3-6d btwn the time of exposure to the antigen and the appearance of antibodies specific for that antigen in the plasma.
    c. During this lag period clonal selection and antibody production both take place.

   d. Plasma antibody levels peak at about 10d and then decline.
   e. B/c the primary immune response results in memory cell production, it will differ from future responses.
   f. In the secondary response, the presence of memory cells primed for the original antigen will result in:
      i. A shorter lag time.
      ii. Plasma cells that remain alive and functioning for a much longer time.
      iii. Achievement of higher antibody levels in a shorter time.
      iv. Higher efficiency of binding between antibodies and antigens.
   g. A similar form of immunological memory will occur with T cells.

24. Classification of Immunity
   a. Active immunity is the result of memory cell production by the body in response to a foreign antigen.
   b. Passive immunity occurs when antibodies from another person (or animal) are transferred to a non-immune individual.
   c. Active immunity can be naturally adaptive in response to infection.
   d. It can also be artificially adaptive due to vaccination – the injection of dead or weakened pathogens into the body. This results in memory cell production, but spares the body of symptoms.
   e. Active immunity lasts for as long as the memory cells remain alive in the body.
   f. Truly long lasting immunity may require continual exposure to the pathogen.
   g. Passive immunity, since it does not involve memory cell production, has a much shorter duration than does active immunity – lasting only as long as the antibodies remain in the circulation.
   h. Passive immunity can be natural when antibodies cross the placenta and travel from the maternal bloodstream to the fetal bloodstream, or when antibodies are excreted in breast milk.
   i. It can be artificial when antibodies are given by injection.

25. Regulatory T Lymphocytes
   a. Function to rein in the responses of B and T cells and make sure they do not go overboard.